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From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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VOSSIUS & PARTNER
Siebertstrasse 4
81675 München
ALLEMAGNE

EINGEGANGEN
Vossius & Partner
24. Sep. 2001
Frist 21.12.
bearb.. 21.10.

WRITTEN OPINION

(PCT Rule 66)

Date of mailing *(day/month/year)*	21.09.2001
Applicant's or agent's file reference F 1750 PC	**REPLY DUE** **within 2 month(s)** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/26948	29/09/2000	01/10/1999

International Patent Classification (IPC) or both national classification and IPC

C12N15/86

Applicant

GENOVO, INCORPORATED et al.

1. This written opinion is the first drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☒	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☒	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain document cited
VII	☐	Certain defects in the international application
VIII	☐	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 01/02/2002.

Name and mailing address f the International preliminary examining authority:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized fficer / Examiner
Renggli-Zulliger, N

Formalities fficer (incl. extension of time limits)
Cleere, C
Telephone No. +49 89 2399 7713

I. Basis f th opinion

1. With regard to the elem nts of the international application (Replacement *sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*):

Description, pages:

1-66 as originally filed

Claims, No.:

1-24 as originally filed

Drawings, sheets:

1/10-10/10 as originally filed

Sequence listing part of the description, pages:

1-3, filed with the letter of 21.12.00

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☒ furnished subsequently to this Authority in written form.
- ☒ furnished subsequently to this Authority in computer readable form.
- ☒ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☒ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 22, 23,

because:

   ☒ the said international application, or the said claims Nos. 22, 23 relate to the following subject matter which does not require an international preliminary examination (*specify*):
   see separate sheet

   ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos. .

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the standard.

   ☐ the computer readable form has not been furnished or does not comply with the standard.

IV. Lack of unity of invention

1. In response to the invitation (Form PCT/IPEA/405) to restrict or pay additional fees, the applicant has:

   ☐ restricted the claims.

☐ paid additional fees.

☐ paid additional fees under protest.

☐ neither restricted nor paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with for the following reasons and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees:
see separate sheet

3. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this opinion:

☒ all parts.

☐ the parts relating to claims Nos. .

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	19-23
Inventive step (IS)	Claims	1-24
Industrial applicability (IA)	Claims	

2. Citations and explanations
see separate sheet

Re Item III

Non-establishm nt of opinion with regard to novelty, inventive step and industrial applicability

Claims 22, 23 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item IV

Lack of unity of invention

The lack of unity as formulated in the search report (IPER:PCT/ISA/210) is maintained. However, both inventions have been examined, since the second invention (claims 19-23) could be examined without effort justifying an additional fee.

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: US-A-5 780 280 (MCNALLY MAUREEN A ET AL), 14 July 1998.

D2: WO 98 46728 A (UNIV NORTH CAROLINA ;CELL GENESYS INC (US)) 22 October 1998, cited in the application.

D3: WO 96 13598 A (UNIV PENNSYLVANIA ;WILSON JAMES M (US); FISHER KRISHNA J (US); KEL), 9 May 1996.

D4: KYOSTIO S R M ET AL: 'Negative regulation of the Adeno-Associated Virus (AAV) P5 promoter involves both the P5 Rep binding site and the consensus ATP-binding motif of the AAV Rep68 protein.' J. VIROL., vol. 69, no. 11, November 1995, pages 6787-6796, XP002158144 .

D5: WANG X S & SRIVASTAVA A: 'Rescue and autonomous replication of Adeno-Associated Virus Type 2 genomes containing Rep-binding site mutations in the viral P5 promoter.' J. VIROL., vol. 72, no. 6, June 1998 , pages 4811-4818, XP002158145.

Novelty (Article 33(1) and (2) PCT)

1) Claims 19-23 attempt to define the subject-matter in terms of "a product by process". Such a formulation is only allowable under specific circumstances if the product cannot be defined by a clear technical feature, this not the case here. The simple fact that a product is obtained by a certain process does not make it different and thus novel over the same product obtained by another process. rAAV, purified or in a lysate are well known compounds. The fact that a the recombinant AAV is obtained by an alternative process does not render the product itself novel over the prior art (D1-D5). Therefore, the subject-matter of claims 19-23 is not novel.

2) The subject-matter of claims 1-18 and 24 is novel in view of the cited prior art, because adenovirus vectors for the manufacture of rAAV comprising AAV rep and cap genes in which the p5 promoter is deleted upstream of the AAV rep gene is not disclosed.
It is noted that claim 24 was examined as if it was dependent on claims 1-11, since a product claim cannot be dependent on a claim of a different category i.e. a method claim.

Inventive step (Article 33(1) and (3) PCT)

3) The subject-matter of claims 1-18 and 24 does not involve an inventive step for the following reasons:
Document D1, which is considered to be the closest prior art, discloses an adenovirus vector to produce a recombinant AAV comprising the AAV rep and cap gene under the control of the P5 promoter as well as the method using this vector.

The difference between D1 and the present application is the deletion of the p5 promoter upstream from the AAV rep gene of the adenovirus vector.

In view of D1, the problem to be solved is to provide an alternative adenoviral vector for the manufacture of rAAV.

The solution proposed by the present application is to remove the p5 promoter.

From D2, it is clear that the in order to increase the efficiency of recombinant AAV the

promoter p5 upstream of the AAV rep gene should be removed. This is also emphasized in D4 and D5.

Consequently, in view of D1 in combination with D2, it was obvious to delete p5. Therefore, subject-matter of claims 1-18 and 24 does not involve an inventive step.

It can also be derived from D1 in combination with D4 or D5 that the subject-matter of claims 1-18 and 24 does not involve an inventive step.

Industrial applicability (Article 33(1) and (4) PCT)

4) For the assessment of the present claims 22, 23 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.